

Cancer 'Cure' Has Limitations

By Joshua Lederberg

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"CURE-CANCER!" a crusade now well-launched with President Nixon's acclaim, has come under skeptical fire. The slogan does warrant careful analysis. Like all war cries, it is an oversimplification, and it has some potential for backfiring if unachievable hopes are aroused.

It is also a subject on which honest men may disagree; but with so much at stake, the public interest might be well served by encouraging the most optimistic in each facet of the cancer problem to prove that his is the true solution. If any one is successful, we will all benefit.

We should not dismiss the fact that some \$2 billion has already been invested in cancer research in the last 20 years. What is the outcome?

Earlier diagnosis of certain cancers, and new treatments by surgery, radiation and drugs, have reduced the inevitability of dying from a cancer, once found. More than two million citizens who have had cancer would not be alive today had they been left untreated.

Nevertheless, the aggregate rate of death from cancer is still rising, mainly because of lung cancer cases attributable to cigarette smoking and air pollution. Can more money spent on research give us a realistic hope of outpacing these statistics?

There is certainly need for wider availability of the measures already available at the best-staffed centers, but we simply do not have the basic knowledge to do more than gain time with many cancers after they have reached a certain state of development. At the present time, about one person in six dies of cancer; the best available (and costly) treatments probably could not improve that figure below one in ten. This would be a notable accomplishment, but it would buy

fewer lives per dollar spent than many other unmet opportunities.

Some specific exceptions should not be forgotten. They include vigorous treatment of some leukemias with new drugs, and the sophisticated use of new forms of radiation for the eradication of Hodgkin's disease. They also include some mass screening programs for the early detection of cancer of the cervix and of the breast, which verge on other measures for prevention rather than cure.

A Broader Attack

THE DISSEMINATION of existing modes of treatment has another payoff besides giving every cancer patient a chance to get the best in available therapy. It would broaden the base of research on human cancer, for the improvement of the methods and the testing of totally new concepts. Given a cost-effective balance between more care and more knowledge, many of the proposed new cancer centers may be effective investments.

The greatest promise, of course, comes from the great leaps in basic biological knowledge of the last decade, many of them in the related areas of DNA and viruses. These have so far given only a few answers centrally connected with human cancer, but we are now able to formulate sensible questions about the nature of the cancer cell and the origin of its deadly differences from the normal.

These were only dimly perceived before now, and were far beyond the reach of our experimental tools. Within the last few months, however, we have learned that tumor viruses in animals produce a remarkable enzyme that codes DNA from RNA, the reverse of the process by which the genes control normal development.

Furthermore, this special enzyme has also been found in cells of human leukemia, previously suspected, but not otherwise proven, to be caused by a virus. (These viruses may be harbored by most normal individuals; we

are not speaking of a contagious disease like influenza.) Naturally, many investigators are probing the properties of this enzyme in search of approaches to block its activity, say with a specific drug or with some competing viruses otherwise harmless.

Despite these leads, I believe that "Cure Cancer" is a misleading slogan, but only because cancer prevention is a far more promising approach than the cure of the disease once established. Prevention also offers the most incisive channels for exploiting basic molecular and cell biology.

It is not as glamorous as cure by surgery or radiation, and a citizen who may balk at another dollar's outlay for preventive public health will spend a fortune to root out his own cancer after the fact. Human nature, however, still does not exclude the eventual use of rational intelligence to help decide among policy alternatives.

The very facts of changes in cancer incidence in different eras, and in different occupations and geographical areas, give the strongest hopes for preventive measures. For they speak to the importance of specific environmental factors rather than letting us acquiesce ignorantly to cancer as an inevitable lightning bolt.

Many forms of cancer are related to known environmental hazards: asbestos and uranium for lung cancers of different kinds; certain dyestuffs for bladder cancer. Chemists are subject to an increased risk of cancers of the pancreas and lymphoid tissues. Learning the environmental factors responsible here might benefit housewives and amateur photographers even more than the professional laboratory workers, who give crisper data for statistical analysis.

The effective pursuit of these leads will, however, require the linking of various statistics, for example, Social Security data on occupational histories with recorded causes of death. This is now obstructed by a legal impasse

over safeguards of privacy and confidentiality.

Cigarette smoking is, of course, the best known of the environmental factors in the United States. Nevertheless, the surge in lung cancer has not been halted, partly on account of the momentum of decades of innocence; partly on account of psychosocial stupidity in the face of overwhelming evidence, and to a large degree because of unanswered technical questions.

When we learn just how the cigarette works, we might persuade a few more scoffers; more important, we could surely devise a smoke that still satisfied while lacking the naughty thrill implied by the old cliché "coffin nail." Individuals may also differ in their inherent sensitivity to the active ingredients of tobacco. Biochemical tests might then identify the high-risk citizens who should be most energetically dissuaded from smoking, or warned to have their lungs checked as often as they lubricate their cars.

An Inherent Safeguard

RECENT WORK has also thrown light on the role of the immune system, hitherto thought of mainly in connection with infectious diseases like smallpox, polio or diphtheria. We now theorize that many incipient cancers are normally eliminated in the healthy body. However, a weakening of the immune mechanism may allow a potential cancer seed to escape this surveillance and grow to unmanageable size and virulence.

Some drugs used to suppress the immune reaction against organ grafts have been associated with a visibly higher incidence of cancer. Research would aid prevention here by providing the tools to evaluate widely used drugs, for we do not know how to test them properly at this time. It could also establish the role of genetic factors or of other disease conditions in weakening the immune response.

Thus Burkitt's lymphoma, a leukemia-like disease found across Africa, is

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connected with the coincidence of malaria and infection with a virus related to mononucleosis. Both of these diseases have profound effects on the immune system; neither alone, in all likelihood, will cause the cancer.

When the immune factor in cancer is clarified, we might eventually develop specific vaccines. (In my own view, we are more likely to learn how to tend to the health of the immune system as a bulwark against cancer.)

Another line of action is already well-founded in basic work. This is the evaluation of the direct cancer potential of chemicals used as food additives or drugs or otherwise added to the human environment. Existing methods are costly, and not always foolproof. Perhaps the anticipated shock of discovering how many of our synthetic additives, and perhaps some natural foods as well, have a cancer potential is a greater deterrent than the expense of deeper reliance on these tests.

We know the appropriate directions needed to improve cancer tests. We also know how to set up preliminary screens with much cheaper laboratory models of cancer than colonies of mice, like mutation in bacteria and chemical changes in DNA. We can also tackle the difficult and subtle problems of more accurately translating the results of laboratory tests into quantitative measures of human hazard. This area, more than any other, needs only money to give prompt returns in reducing environmental cancer.

A Social Factor

CHEMICAL TECHNOLOGY is not the only change in modern life style that may be influencing cancer rates. Epidemiological surveys made over a period of many decades suggest that breast cancer occurs most often in women with fewer or no children, or who started childbearing later in life.

A modern social motif that now encourages these trends must also bear the burden of accounting for this subtle side-effect on normal variations in the hormone balance of the body. Present methods of assessing the role of natural hormones, and related synthetic drugs, in animals are all too crude for any reliable use, except to arouse suspicions if cancer-promoting effects are found.

The problems of testing potential cancer-preventing agents in this field are technically formidable. They would involve clinical testing on large numbers of healthy women for the sake of preventing a disease that will eventually attack only about one in 1500. The problem of justifying and financing such kinds of testing has become insuperable for a profit-oriented system of drug development.

To protect the public interest, the drug industry must be policed by the Food and Drug Administration in a way that objectively assumes the utmost venality and unreliability of any member. When profits are involved, the remotest doubts about the safety of a clinical test would have to be resolved against a company. Investment in innovative areas is, however, so discouraged by this philosophy that it will wither away if left to free enterprise.

The answer is not to relax regulatory vigilance but to establish a new system for the development of such preventive measures under direct government control and sponsorship. This is a mandate to undertake drug development as a positive responsibility to balance the regulatory inhibition of private enterprise in this field. The fulfillment of such a mandate, with its attendant legal and political problems, would be enough justification for the National Cancer Authority that has been advocated to establish a "cure" for cancer as a national goal.

Whatever administrative machinery is established to achieve this goal, it must fix a consistency of purpose for health research that has been flawed for the past several years. The rapid changes in our outlook on federal responsibilities for health have outpaced the financing and administrative capacity of the Department of Health, Education, and Welfare. For example, consistent underestimates of the costs of medical care programs, and confusions about the means needed to bolster the supply of health services, have generated predictable budgetary crises. In the struggle for disposable funds, research was bound to be the most vulnerable target for lack of a well-defined political constituency. The new presidential initiatives, coupled with vigorous pressure from the Congress, will happily put the lie to a cynical pessimism about the future of bio-medical research like that expressed in my own writings heretofore.

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